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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/500,447	06/30/2004	Hee-Sung Park	26028	7722

20529 7590 12/11/2006

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EXAMINER	
WORLEY, CATHY KINGDON	
ART UNIT	PAPER NUMBER
1638	

DATE MAILED: 12/11/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/500,447	PARK, HEE-SUNG	
	Examiner	Art Unit	
	Cathy K. Worley	1638	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 June 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-5* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *30 June 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *6/30/04; 6/30/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Specification

1. The specification is objected to because the Brief Description of the Drawings does not include descriptions of each panel included in each figure. Figure 1 has panels A-C and each panel must be described individually. Figure 4 has panels A-D which each must be described individually. Figure 7 has panels A and B which each must be described individually. Figure 8 has panels A and B, and furthermore, within panel A there are panels a-f; each of these panels must be described individually. In addition, the descriptions of Figure 5 and Figure 7 disclose that they are photographs, but they do not disclose what was photographed. The descriptions of these figures should specify how the expression is demonstrated; ie. is it a Western Blot?, a coomassie blue stained gel?, a silver-stained gel?, etc.

2. The use of the following trademarks has been noted in this application: NYTRAN, HYBOND, TWEEN, and WESTERN BLUE. They should be written in all capital letters wherever they appear and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to

prevent their use in any manner which might adversely affect their validity as trademarks.

Claim Objections

3. Claims 2-5 are objected to because of the following informalities: They each recite the limitation "of production" in line 1, however they each depend from claim 1 which utilizes different terminology. The method in claim 1 is a method "for producing recombinant protein" rather than a method "of production". The Applicant is advised to amend claims 2-5 to replace "of production" with - - for producing recombinant protein - - .

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 1-5 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. All dependent claims are including in these rejections.

Claims 1 and 3-5 recite a "gene", and the use of the word "gene renders these claims indefinite because it is unclear if this encompasses the promoter, introns, 3' regulatory sequence, etc. or if it only encompasses the coding region of the gene. If the Applicant intends to encompass only the coding region, then the applicant is advised to amend the claims accordingly.

Claim 1 recites the limitation "target gene" in line 5. There is insufficient antecedent basis for this limitation in the claim. Does this "target gene" encode the recombinant protein? Or does this "target gene" have some other purpose? It is unclear how the target gene is related to the recombinant protein being produced.

Claim 5 is indefinite because it recites "the target gene" which is in the singular, but then follows with two genes, UreB and tPA. Does this mean the pollen is being transformed with two genes simultaneously? Or does this mean the pollen is being transformed with either one or the other gene? Or does this mean the pollen is being transformed with a gene fusion that encodes both proteins?

5. Claim 4 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of producing recombinant protein

using plant pollen, wherein the pollen is transformed via *Agrobacterium* and wherein the nucleic acid encoding the recombinant protein is introduced into *Agrobacterium* by electroporation, does not reasonably provide enablement for said method wherein the nucleic acid is introduced into *Agrobacterium* by particle bombardment or vacuum infiltration. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

The claim is broadly drawn to a method that utilizes transformed *Agrobacterium*, wherein a nucleic acid is introduced into the *Agrobacterium* by particle bombardment, vacuum infiltration, or electroporation.

The nature of the invention is a method of transforming pollen via *Agrobacterium*-mediated transformation.

The art teaches that nucleic acids can be introduced into *Agrobacterium* by electroporation, tri-parental mating, freeze-thaw transformation (see Wise et al. (2006) Methods Mol Biol. Vol. 343, pp. 43-53), and chemical transformation (see Cui et al. (1995) Chin J Biotechnol. Vol. 11, pp. 267-274).

The art does not teach that nucleic acids can be introduced into *Agrobacterium* by particle bombardment or vacuum infiltration.

The instant application discloses that plasmids were introduced into *Agrobacterium* using the freeze-thaw method (see page 8, lines 13-15).

One of ordinary skill in the art would be familiar with the techniques of electroporation, tri-parental mating, freeze-thaw transformation, or chemical transformation, however particle bombardment and vacuum infiltration are not recognized in the art as viable methods of transforming *Agrobacterium.*

Attempting to introduce a nucleic acid into *Agrobacterium* using particle bombardment or vacuum infiltration would be highly unpredictable. Particle bombardment is likely to kill the bacterial cells. Vacuum infiltration would not be likely to get the nucleic acids into the cells. Because neither of these methods is known in the art to work successfully to introduce foreign DNA into *Agrobacterium,* and because there is no direction provided by the inventor in the instant specification, there is a high degree of unpredictability involved in attempting to transform *Agrobacterium* with these methods.

Given the unpredictability in the art, the lack of guidance in the specification, and the fact that there are zero working examples disclosed, it would require undue experimentation on the part of one of skill in the art to be able to practice a method wherein *Agrobacterium* is transformed by particle bombardment or vacuum infiltration.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

6. Claims 1 and 4 are rejected under 35 U.S.C. 102(b) as being anticipated by Burke et al. (US Patent No. 5,929,300, issued on July 27, 1999).

The claims are drawn to a method comprising the steps of isolating pollen from a plant, culturing the pollen, introducing a target gene into *Agrobacterium* by electroporation, infecting the cultured pollen with the *Agrobacterium*, and growing the pollen with the gene.

Burke et al. teach isolation of pollen from a plant (see column 6, lines 55-56). They teach culturing the pollen on a solid medium that supports pollen germination (see column 6, lines 11 and 56-57). This solid medium is a pollen growth medium. They teach introduction of plasmids into *Agrobacterium* by electroporation (see column 6, lines 33-36). These plasmids contain "target genes". They teach inoculation of the pollen with a lawn of *Agrobacterium* (see column 6, lines 46-51). This inoculation is a method of "infecting" the transformed *Agrobacterium* into the cultured plant pollen. They teach growing the pollen to allow for germination and production of transgenic pollen (see column 6, lines 62-67). The recombinant protein was produced as evidenced by the resulting herbicide resistance (see column 7, lines 29-36). In this case the recombinant protein being produced is the phosphinothricin acetyltransferase enzyme encoded by the 35S-bar construct (see column 6, lines 24-27).

7. Claim 1 is rejected under 35 U.S.C. 102(b) as being anticipated by Heberle-Bors et al. (Foreign Patent from Austria: AT 388384, published on June 12, 1989; see translation provided by the USPTO).

The claim is drawn to a method comprising the steps of isolating pollen from a plant, culturing the pollen, introducing a target gene into *Agrobacterium*, infecting the cultured pollen with the *Agrobacterium*, and growing the pollen with the gene.

Heberle-Bors et al. teach the isolation of pollen and cultivating the pollen in AMGLU medium, and they teach co-culturing the pollen with *Agrobacterium* (see first paragraph on page 12). The *Agrobacterium* they utilized comprised the CAT gene coupled to a 35S promoter, and the *Agrobacterium* infected the pollen cells, transferred the foreign DNA into the pollen cells, and resulted in the production of recombinant protein which is evident by the CAT enzyme assay performed on pollen extracts (see second paragraph on page 12).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

8. Claim 2 is rejected under 35 U.S.C. 103(a) as being unpatentable over Fernando et al. (Plant Cell Reports (2000) Vol. 19, pp. 224-228) in view of Heberle-Bors et al. (Foreign Patent from Austria: AT 388384, published on June 12, 1989; see translation provided by the USPTO).

The claim is drawn to a method comprising the steps of isolating pollen from a plant, culturing the pollen, introducing a target gene into *Agrobacterium*, infecting the cultured pollen with the *Agrobacterium*, and growing the pollen with the gene; wherein the pollen is isolated from *Lilium longiflorum* or *Pinaceae*.

Fernando et al. teach a method of transiently expressing GUS in pine pollen (see abstract). Fernando et al. teach the isolation of pollen from *P.monticola* cones (see page 225, left column). *P. moticola* is a member of the *Pinaceae* family. The pollen was cultured in a pollen germination medium (see page 225, left column). Plasmid DNA encoding the GUS reporter was introduced to the pollen grains via particle bombardment (see page 225, right column). The transformed pollen was incubated for 24 hours to allow the expression of the recombinant protein (GUS) (see page 225, right column).

Fernando et al. do not teach the use of Agrobacterium to transfer the foreign DNA into the pollen.

Heberle-Bors et al. teach the use of Agrobacterium to transfer foreign DNA into pollen (see Experiment 7 on pages 12-13).

At the time the invention was made, it would have been obvious and within the scope of one of ordinary skill in the art to modify the method taught by Fernando et al. to utilize Agrobacterium to transfer the foreign DNA into pollen as taught by Heberle-Bors et al. One of ordinary skill would have been motivated by the teaching of Heberle-Bors et al. that their method can be utilized to successfully transform plants in which successful gene transfer has not been possible in the past (see page 5, second paragraph), such as trees and forest plants (see second paragraph on page 5 and paragraph bridging pages 6-7); and by the teaching of successful transformation of *Pinaceae* by Fernando, one would have a reasonable expectation of success given the success of Fernando and Heberle-Bors.

9. Claim 3 is rejected under 35 U.S.C. 103(a) as being unpatentable over Heberle-Bors et al. (Foreign Patent from Austria: AT 388384, published on June 12, 1989; see translation provided by the USPTO).

The claim is drawn to a method comprising the steps of isolating pollen from a plant, culturing the pollen, introducing a target gene into *Agrobacterium*, infecting the cultured pollen with the *Agrobacterium*, and growing the pollen with the gene, wherein a specific growth medium is utilized.

The pollen growth medium taught by Heberle-Bors et al. is the AMGLU medium which comprises Miller's macrosalts (KNO_3, NH_4NO_3, $Ca(NO_3)_2 \cdot 4\ H_20$, KH_2PO_4, KCl, and $MgSO_4 \cdot 7\ H_2O$), MS microsalts ($MnSO_4 \cdot 4\ H_20$, $ZuSO_4 \cdot 7\ H_2O$,

H_3BO_3, KI, $Na_2MoO_4 \cdot 2\ H_2O$, $CuSO_4 \cdot 5\ H_2O$, $CoCl_2 \cdot 6\ H_20$), sucrose, and glutamine (see pages 13-14).

The instant claim 3 recites 5-10% sucrose, and Heberle-Bors et al. teach 0.25M sucrose which is 8.6% w/v. The instant claim 3 recites 0.5-3 mM $Ca(NO_3)_2$, and Heberle-Bors et al. teach 347 mg/liter of the tetra hydrate which is 1.5 mM. The instant claim 3 recites 50-300 μM H_2BO_3, and Heberle-Bors et al. teach 6.2 mg/liter of H_3BO_3 which is the protonated version of H_2BO_3, and 6.2 mg/liter of H_3BO_3 is 100 μM. The instant claim 3 recites 0.001-5 mM KNO_3, and Heberle-Bors et al. teach 1,000 mg/liter which is 9.9 mM. The instant claim 3 recites 0.1-10 mM KH_2PO_4, and Heberle-Bors et al. teach 300 mg/liter which is 2.2 mM.

Therefore, Heberle-Bors et al. have taught all of the components in the medium recited in claim 3.

Heberle-Bors et al. did not teach a medium "composed of" the recited elements because the medium they taught contained additional elements and further the medium they taught had 9.9 mM KNO_3, which is above the range recited in the instant claim 3.

At the time the invention was made, it would have been obvious and within the scope of one of ordinary skill in the art to optimize the process parameters to determine and use the minimal components required for successful pollen growth (*de minimus* optimization). One would have been motivated to do so because it

would result in a medium that is less complex, faster and easier to make, and less expensive.

10. Claim 5 is rejected under 35 U.S.C. 103(a) as being unpatentable over Heberle-Bors et al. (Foreign Patent from Austria: AT 388384, published on June 12, 1989; see translation provided by the USPTO) in view of each of Brodzik et al. (Food Biotechnology (2000) Editors: Bielecki, Tramper and Polak; Elsevier Science, pp. 35-42) and Becker et al. (Proc. of the Phytochem. Soc. of Europe (1993) Vol. 35, pp. 325-331).

The claim is drawn to a method comprising the steps of isolating pollen from a plant, culturing the pollen, introducing a target gene into *Agrobacterium*, infecting the cultured pollen with the *Agrobacterium*, and growing the pollen with the gene, wherein the target gene is UreB gene from *Helicobacter pylori* and tissue plasminogen activator (tPA) from humans.

Heberle-Bors et al. teach the transformation of pollen and production of recombinant protein in the pollen (see 102(b) rejection above).

Heberle-Bors et al. do not teach the production of recombinant UreB or tPA.

Brodzik et al. teach the production of recombinant UreB from *Helicobacter pylori* in transgenic plants (tobacco and carrots) (see abstract, page 39, and page 41, figure 5).

Becker et al. teach the production of recombinant human tPA in transgenic tobacco seeds (see page 329, Figure 22.4).

At the time the invention was made, it would have been obvious and within the scope of one of ordinary skill in the art to modify the method taught by Heberle-Bors et al. to produce UreB (taught by Brodzik et al.) or to produce tPA (taught by Becker et al.). One would have been motivated to produce UreB because Brodzik et al. teach that UreB is a promising candidate for a vaccine against the bacteria that causes chronic active gastritis (see page 36, second paragraph). One would have been motivated to produce tPA because Becker et al. teach that it is a therapeutically important protein (see last paragraph on page 325), and would have a reasonable expectation of success given the success of Heberle-Bors, Brodzik, and Becker.

11. All claims are rejected.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Cathy K. Worley whose telephone number is (571) 272-8784. The examiner is on a variable schedule but can normally be reached on M-F 10:00 - 4:00 with additional variable hours before 10:00 and after 4:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anne Marie Grunberg, can be reached on (571) 272-0975. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

CKW
Nov. 24, 2006

RUSSELL P. KALLIS, PH.D.
PRIMARY EXAMINER

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